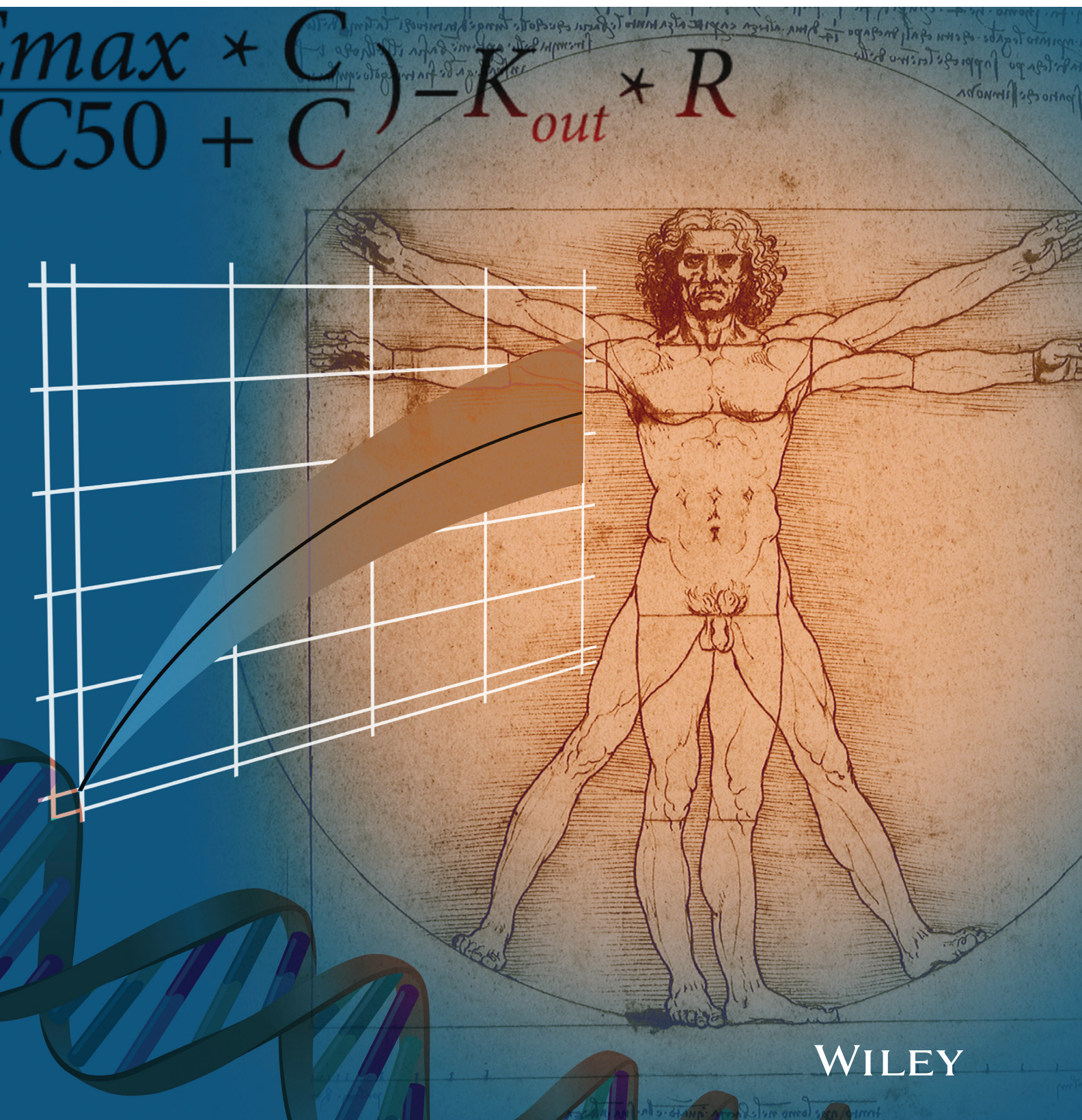


An Official Journal of ASCPT and ISoP

CPT: Pharmacometrics & Systems Pharmacology

Open Access



WILEY

Editor-in-Chief

France Mentré, MD, PhD, *School of Medicine of University Paris Diderot, Paris, France*

Deputy Editor-in-Chief

Lena Friberg, PhD, *Uppsala University, Uppsala, Sweden*

Associate Editors

Jonathan French, ScD, *Metrum Research Group, Tariffville, CT, USA*
Stefanie Hennig, MSc, PhD, *Certara Strategic Consulting, Brisbane, Australia*
Sriram Krishnaswami, PhD, *Pfizer, Groton, CT, USA*
Vikram Sinha, PhD, *Takeda Pharmaceuticals International Co., Cambridge, MA, USA*
Ping Zhao, PhD, *Bill & Melinda Gates Foundation, Seattle, WA, USA*
Eric Sobie, PhD, *Icahn School of Medicine at Mount Sinai, New York, NY, USA*
Karen Rowland Yeo, PhD, *Certara UK Ltd., Sheffield, UK*

Editors-in-Training

Vivaswath S. Ayyar, PhD, *Janssen Research & Development, Spring House, PA*
Natasha Strydom, PhD, *University of California San Francisco, San Francisco, CA*

American Society for Clinical Pharmacology and Therapeutics

Chief Executive Officer

Sharon J. Swan, *Alexandria, VA*

Chief Operating Officer

Elise S. Laffman-Johnson, *Alexandria, VA*

Managing Editor

Alethea B. Gerding, *Alexandria, VA*

Deputy Managing Editor

Alaina Webster, *Alexandria, VA*

Editorial Coordinator

Aimee Greene, *Alexandria, VA*

Editorial Board

Ioannis Androulakis, PhD, *Rutgers University Surgery, UMDNJ-RWJ Medical School Piscataway Township, NJ, USA*

Joseph P Balthasar, PhD, *University of Buffalo Buffalo, NY, USA*

Robert Bies, PharmD, PhD, *Indiana University Bloomington, IN, USA*

Marc Birtwistle, PhD, *Clemson University Clemson, SC, USA*

Marylore Chenel, PharmD, PhD, *Institut de Recherches Internationales Servier Suresnes, France*

Paolo Denti, PhD, *University of Cape Town Cape Town, South Africa*

James M. Gallo, PharmD, PhD, *Albany College of Pharmacy and Health Sciences, Albany, NY, USA*

Christine Garnett, PhD, *US Food and Drug Administration, Silver Spring, MD, USA*

Ekaterina Gibiansky, PhD, *QuantPharm LLC North Potomac, MD, USA*

Manish Gupta, PhD, FCP, *GenMab; Princeton, NJ, USA*

Bart Hendriks, PhD, *Merrimack Pharmaceuticals Cambridge, MA, USA*

Nicholas H.G. Holford, MBChB, *The University of Auckland Auckland, New Zealand*

Brett Howell, PhD, *The Hamner-UNC Institute for Drug Safety Sciences Research Triangle Park, NC, USA*

Kristin Karlsson, PhD, *Uppsala University Uppsala, Sweden*

Ron Keizer, PhD, *InsightRX San Francisco, CA, USA*

Steven E. Kern, PhD, *Bill & Melinda Gates Foundation Seattle, WA, USA*

Andrzej Kierzek, PhD, *Certara QSP; Sheffield, United Kingdom*

Wei Lu, PhD, *Peking University/Pfizer Pharmacometrics Beijing, China*

Rajanikanth Madabushi, PhD, *US Food and Drug Administration, Silver Spring, MD*

Efthymios Manolis, MSc, *European Medicines Agency London, United Kingdom*

Peter Milligan, PhD, *Pfizer Global Research and Development London, United Kingdom*

Kyungsoo Park, MD, PhD, *Yonsei University College of Medicine Seoul, Republic of Korea*

Marc Pfister, MD, FCP, *University of Basel Basel, Switzerland*

Jose Pinheiro, PhD, *Johnson and Johnson Pharmaceutical Research Raritan, NJ, USA*

Benjamin Ribba, PhD, *F. Hoffman-La Roche, Basel, Switzerland*

Julio Saez-Rodriguez, PhD, *RWTH Aachen University, Aachen, Germany*

Radojka Savic, PhD, *University of California Oakland CA, USA*

Virginia D. Schmith, PhD, FCP, *GlaxoSmithKline Zebulon, NC, USA*

Daniel Scholes Rosenbloom, PhD, *Merck & Co., New York, NY, USA*

Joe Standing, PhD, *University College London London, United Kingdom*

Yuichi Sugiyama, PhD, *Riken Innovation Center Sugiyama Laboratory Yokohama, Japan*

Joel Tarning, PhD, *Mahidol-Oxford Tropical Medicine Research Unit Bangkok, Thailand*

Nicholas Tatonetti, PhD, *Columbia University New York, NY, USA*

Paolo Vicini, PhD, MBA, *MedImmune, Cambridge, United Kingdom*

Hua Xu, PhD, *University of Texas Health Science Center Houston, Texas, USA*

Ping Zhang, PhD, *IBM T. J. Watson Research Center Yorktown Heights, NY, USA*

Overview

CPT: Pharmacometrics & Systems Pharmacology (PSP) is an official open access journal of the American Society for Clinical Pharmacology and Therapeutics (ASCPT) and International Society of Pharmacometrics (ISoP).

CPT: Pharmacometrics & Systems Pharmacology is a cross-disciplinary journal devoted to publishing advances in quantitative (e.g., modeling and simulation) methods as applied in pharmacology, physiology and therapeutics in humans. The journal welcomes original research articles, reviews and tutorials that bridge the following areas: pharmacometrics, modeling and simulation as applied to the design and evaluation of clinical trials, systems pharmacology modeling, particularly with a mechanistic link to human (patho)physiology, disease modeling, “population” or mixed-effects pharmacokinetics and pharmacodynamics (PKPD) modeling, modeling and simulation to support translational research, physiologically-based pharmacokinetics (PBPK), model-based meta-analyses of clinical trials, mechanism-based pharmacokinetic-pharmacodynamic modeling, computational pharmacology, bioinformatics, comparative efficacy, effectiveness and cost-effectiveness. Systems pharmacology may involve the application of systems biology approaches to study drug activities, targets and effects. The discipline is often defined with reference to engineering and pharmacological principles as the quantitative analysis of the dynamic interactions between drugs and a biologic system that aims to understand the behavior of the system as a whole. The common focus will be on quantitative methods that improve our understanding of pharmacology and therapeutics in humans.

Abstracting and Indexing

- Embase (Elsevier)
- SCOPUS (Elsevier)
- MEDLINE/PubMed indexing

Society Information

The American Society for Clinical Pharmacology and Therapeutics (ASCPT) was founded in 1900, and consists of over 2,200 professionals whose primary interest is to advance the science and practice of clinical pharmacology and translational medicine for the therapeutic benefit of patients and society. ASCPT is the largest scientific and professional organization serving the disciplines of Clinical Pharmacology and Translational Medicine.

All articles published in this journal are freely available to read, download, and share. Articles are published under the terms of the Creative Commons Attribution Non-Commercial License which permits use, distribution, and reproduction in any medium, provided the original work is properly cited and is not used for commercial purposes.

Disclaimer

The Publisher, the American Society for Clinical Pharmacology and Therapeutics, the International Society of Pharmacometrics, and Editors cannot be held responsible for errors or any consequences arising from the use of information contained in this journal; the views and opinions expressed do not necessarily reflect those of the Publisher, the American Society for Clinical Pharmacology and Therapeutics, the International Society of Pharmacometrics, and Editors, neither does the publication of advertisements constitute any endorsement by the Publisher, the American Society for Clinical Pharmacology and Therapeutics, the International Society of Pharmacometrics, and Editors of the products advertised.

Publisher

CPT: Pharmacometrics & Systems Pharmacology is published by Wiley Periodicals, Inc., 101 Station Landing, Suite 300, Medford, MA 02155; Telephone: 781-388-8200; Fax: 781-388-8210.

CPT: Pharmacometrics & Systems Pharmacology

PERSPECTIVES

LETTER TO THE EDITOR

- 393** Modeling is data driven: Use it for successful virtual patient generation
Theodore R. Rieger, Richard J. Allen and Cynthia J. Musante

RESPONSE LETTER TO THE EDITOR

- 395** Response to 'Modeling is data driven: Use it for successful virtual patient generation'
Stephen B. Duffull and Abhishek Gulati

PERSPECTIVE

- 396** Mechanistic models for hematological toxicities: Small is beautiful
Laure Deyme, Sébastien Benzekry and Joseph Ciccolini

REVIEWS

REVIEW

- 399** Physiologically-based pharmacokinetic modeling to support bioequivalence and approval of generic products: A case for diclofenac sodium topical gel, 1%
Eleftheria Tsakalozou, Andrew Babiskin and Liang Zhao

MINI-REVIEWS

- 412** Quantitative systems pharmacology in neuroscience: Novel methodologies and technologies
Peter Bloomingdale, Tatiana Karelina, Murat Cirit, Sarah F. Muldoon, Justin Baker, William J. McCarty, Hugo Geerts and Sreeraj Macha
- 420** Opening a debate on open-source modeling tools: Pouring fuel on fire versus extinguishing the flare of a healthy debate
Amin Rostami-Hodjegan and Frederic Y. Bois

RESEARCH

ARTICLES

- 428** Translational pharmacokinetic-pharmacodynamic modeling of preclinical and clinical data of the oral MET inhibitor tepotinib to determine the recommended phase II dose
Wenyuan Xiong, Manja Friese-Hamim, Andreas John, Christopher Stroh, Manfred Klevesath, Gerald S. Falchook, David S. Hong, Pascal Girard and Samer El Bawab
- 441** Comprehensive PBPK model to predict drug interaction potential of Zanubrutinib as a victim or perpetrator
Kun Wang, Xueting Yao, Miao Zhang, Dongyang Liu, Yuying Gao, Srikumar Sahasranaman and Ying C. Ou
- 455** Physiologically-based pharmacokinetic modeling to predict drug interactions of lemborexant with CYP3A inhibitors
Takashi Ueno, Yukiko Miyajima, Ishani Landry, Bojan Lalovic and Edgar Schuck
- 467** Population pharmacokinetic modeling and simulation to support qualification of pyridoxic acid as endogenous biomarker of OAT1/3 renal transporters
Amais Ahmad, Kayode Ogungbenro, Annett Kunze, Frank Jacobs, Jan Snoeys, Amin Rostami-Hodjegan and Aleksandra Galetin
- 478** Pharm-AutoML: An open-source, end-to-end automated machine learning package for clinical outcome prediction
Gengbo Liu, Dan Lu and James Lu
- 489** Quantitative systems pharmacology model of thrombopoiesis and platelet life-cycle, and its application to thrombocytopenia based on chronic liver disease
Ryosuke Shimizu, Takayuki Katsube and Toshihiro Wajima
- 500** Integrative chemogenomic analysis identifies small molecules that partially rescue $\Delta F508$ -CFTR for cystic fibrosis
Rachel A. Hodos, Matthew D. Strub, Shyam Ramachandran, Ella A. Meleshkevitch, Dmitri Y. Boudko, Robert J. Bridges, Joel T. Dudley and Paul B. McCray Jr.
- 511** Tumor growth inhibition modeling of individual lesion dynamics and interorgan variability in HER2-negative breast cancer patients treated with docetaxel
Sreenath M. Krishnan, Sofiene S. Laarif, Brendan C. Bender, Angelica L. Quartino and Lena E. Friberg